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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/643,450	08/19/2003	Bernhard Hermann Heinrich Breier	ERNZ-01018US1	4401

23910 7590 11/28/2006

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EXAMINER

KOSAR, ANDREW D

ART UNIT	PAPER NUMBER
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1654

DATE MAILED: 11/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/643,450	Applicant(s) BREIER ET AL.	
	Examiner Andrew D. Kosar	Art Unit 1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 September 2006 and 19 July 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) 4,8,12-18,21 and 22 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3,5-7,9-11,19,20 and 23-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Amendment/Arguments

Applicant's amendments and arguments filed July 19, 2006 and on September 14, 2006 are acknowledged and have been fully considered.

Any rejection and/or objection not specifically addressed is herein withdrawn.

Claims 4, 8, 12-18, 21 and 22 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on November 11, 2005.

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. A certified copy of NZ 520,866 was received by the Office on September 14, 2006.

Acknowledgment is made of applicant's claim for foreign priority under 35 USC §§ 119(a)-(d). The certified copy has been filed in Application No. 10/450,232, filed on June 10, 2003.

Applicant's arguments with regards to the claim of priority have been fully considered, and have been found persuasive.

Accordingly, the rejections of claims 1-3, 6, 7, 9, 11 and 23 under 35 USC § 102(b) as anticipated by IKENASIO and the rejection of claims 1-3, 5-7, 9-11, 23 and 25 under 35 USC § 102(b) as anticipated by VICKERS are herein withdrawn, as in view of the perfected claim of priority, the applied references are no longer applicable as prior art.

Applicant's have amended the claims to include the limitation "mammal subject to fetal programming, having a history of..." and argue that the new limitation is neither taught nor

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suggested by the prior art, alone or in combination and that the new limitation distinguished the instant claims over the prior art. Applicant's arguments and amendments have been fully considered, but have not been found persuasive for the reasons set forth below.

Respectfully, Applicant's amendments to distinguish the patient population over the prior art is ineffective. The amendment does not necessarily require that the patient actually have been fetally programmed, but rather that the patient merely be 'subject to' the programming. Furthermore, assuming *arguendo* that the claims are amended to specifically require the patient to have the programming conditions, this would not necessarily distinguish over the prior art. For example, the prior art teaches administration to a hypertensive pregnant mammal. Allegedly, in the fetal programming theory, hypertension is a result of fetal programming. Thus, one could conclude that the hypertensive patient must have been subject to fetal programming.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 5-7, 9-11, 19, 20 and 23-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites, "subject to..." and "associated with" which render the claims vague and indefinite. It is unclear whether the subject must have the fetal programming or under what conditions one would know if the subject had been programmed. Further, it is unclear how the reduction in receptors is 'associated with' decreased systolic blood pressure, i.e.- does it result in the decrease or is it a result of the decrease?

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The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5-7, 9-11, 19, 20, 23, 25 and 26 remain rejected under 35 U.S.C. 102(b) as being anticipated by CLARK (US Patent 5,565,428).

Clark teaches that , “In addition, [ACE] inhibitors may be beneficial in conjunction with the IF-I treatment of renal disorders.” (column 11, lines 37-39), and that “In the treatment of [CHF], ACE inhibitors may be useful together with IGF-I by reducing systemic vascular resistance and relieving circulatory congestion.” (column 11, lines 40-43).

Clark teaches that the ACE inhibitors that can be used include quinapril, ramipril, captopril, benazepril, folinopril, lisinopril and enalapril. (column 11, lines 44-50).

Clark teaches that “Renal function can be enhanced by administration of IGF-I at 100 µg/kg subcutaneously each day”(column 12, lines 54-55).

Because Clark teaches the combination and that the IGF-I is administered within the instantly claimed dose range that is claimed, the administration inherently would modulate the density and/or distribution of angiotensin II receptors as instantly claimed and decrease systolic blood pressure.

Claims 1-3, 5-7, 9-11, 23, 25 and 26 remain rejected under 35 U.S.C. 102(b) as being anticipated by GLUCKMAN (US Patent 5,922,673).

Gluckman teaches a method for treating a pregnant mammal (including a human) via administration of IGF-I or an analog. In humans, the dose is administered at 40-200 µg/kg/day (column 2, lines 1-5).

Gluckman teaches that IGF-I can be administered alone or in combination with another antihypertensive treatments (column 2, lines 15-17).

Gluckman teaches that the IGF-I can be administered by implant, subcutaneous, intramuscular, intranasal or oral routes of administration (column 2, lines 6-14).

Gluckman teaches treating hypertension in a pregnant mammal with IGF-I or an analogue of IGF-I (claim 1), with IGF (claim 5) and IGF at doses of 40-2000 $\mu\text{g/kg}$ and 40-200 $\mu\text{g/kg}$ (claims 10 and 11) and in combination with an other antihypertensive (claim 13).

Because the same compound is being administered and at the same doses as instantly claimed, in practicing the method of Gluckman, one would inherently be practicing the instantly claimed method.

Claims 1, 3, 6, 7, 9-11, 23 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by WILLIAMS (WO 95/17204 A1, for clarity in distinguishing between this reference and Gluckman, *supra*, the secondary author is cited here).

Williams teaches administration of GPE to mammals (e.g. claim 2), as a pharmaceutical (claim 10), orally, IV, subcutaneously, IP, IM, or inhalation (claim 16) and at a dose of 1 μg to about 100 mg/kg/day (claim 20). In looking to the specification, it is noted that the doses administered to the test subjects were 2 to 200 μg (Example 5, page 19), and in other instances 'preferably' 1 mg/kg (Example 2, page 18).

Because the same compound is being administered and at doses of an overlapping range, with doses described in the specification within the instantly claimed range, in practicing the method of Williams, one would inherently be practicing the instantly claimed method.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 5-7, 9-11, 19, 20 and 23-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over GLUCKMAN, as applied to claims 1-3, 5-7, 9-11, 19, 20, 23, 25 and 26, *supra*, in view of CLARK, as applied to claims 1-3, 5-7, 9-11, 19, 20, 23, 25 and 26, *supra*, WILLIAMS, as applied to claims 1, 3, 6, 7, 9-11, 23 and 24, *supra*, DIMARCHI and AMBLER.

The instant claims are presented *supra*.

The teachings of Gluckman, Clark and Williams are presented *supra*.

Ambler teaches, "Although the studies to be discussed herein concentrate on the use of IGF-1, the claims extend to IGF-2 and analogues of IGF-1 and IGF-2 as these are known to exert a similar biological effect to IGF-1 (Schoenle et al., Acta Endoc. 108: 167-174, 1985)." And "By "analogues" of IGF-1 and IGF-2 is meant compounds having the same therapeutic effect as IGF-1 or IGF-2 in humans and animals. These can be naturally occurring analogues of IGF-1 or IGF-2 (eg truncated IGF-1 or DES 1-3 IGF-1 synthesized by GENENTECH, INC. and KABI PHARMACIA) or any of the known synthetic analogues of IGF-1 and IGF-2." (column 3, lines 47-58).

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Williams further teaches the tripeptide GPE is a truncated form of IGF, synthesized or produced after proteolytic cleavage of IGF-1, and that GPE functions like IGF-1 (throughout). Thus, because it functions like IGF-1, it is considered an analog, as defined by Ambler.

DiMarchi teaches IGF-1 analogs, and production of IGF-1, or analogs, through recombinant means (e.g. column 9, line 44+) and recombinant synthesis of human IGF-1 (e.g. citing Ueda, US Patent 5,019,500, column 8, lines 1-3).

DiMarchi teaches treating an individual afflicted with a condition selected from diabetes, diabetic neuropathy, insulin-resistance, IGF-resistance, and other conditions, via administration of an IGF-1 analog (claim 8).

DiMarchi teaches that the dose administered is between 1 and 1000 $\mu\text{g/kg}$ (column 12, line 13+).

The difference between the instant claims and that which is taught by the references, is that while the art teaches administration of IGF-I analogs, the art does not teach the specifically recited IGF-I compounds of claim 24, except GPE.

It would have been obvious to one of ordinary skill in the art to have administered any analog of IGF-1 or IGF-2, alone or in combination with an ACE inhibitor, with the expectation of having a similar outcome from compounds that are considered to be analogs, as defined by Ambler.

One would have been motivated to have practiced the method with any IGF-1 or IGF-2 analog as the methods of Gluckman and DiMarchi can be practiced with any IGF-1 or analog, and because IGF-I analogs are well known in the art to be compounds that act like IGF.

One would have had a reasonable expectation for success in practicing the methods of Gluckman and DiMarchi with any analog, as analogs of IGF-I and IGF-2 are known in the art to have a similar effect to IGF-1 and IGF-2.

With regards to the composition which is administered (IGF-1 and an ACE inhibitor): As set forth in *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980), "It is *prima facie* obvious to combine two compositions each of which is taught by prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose; the idea of combining them flows logically from their having been individually taught in prior art."

In the instant case, IGF-1 and ACE inhibitors are known to be co-administered to treat renal disorders, and thus it would have been obvious to make and use a combination therapy of an IGF and ACE inhibitor.

With regards to administration: It would have been obvious to administer a composition of IGF-1, or an analog, and any ACE inhibitor, including captopril, for the at least additive effect achieved by their co-administration. One would have been motivated to administer both IGF-1 and an ACE inhibitor for the benefit of increased efficacy in treating a, with a reasonable expectation for success in treating a renal disorder, and thus, in treating a renal disorder, one would intrinsically be modulating the density and/or distribution of angiotensin II receptors.

With regards to the doses administered, the references cited above teach administration of IGF-1 or an IGF-1 analog at various doses. It would have been obvious to one skilled in the art at the time of invention to determine all optimum and operable conditions (e.g. dose administered), because such conditions are art-recognized result-effective variables that are routinely determined and optimized in the art through routine experimentation. ("[W]here the

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general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). *See* MPEP § 2145.05).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

NO CLAIMS ARE ALLOWED.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.


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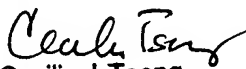
This application contains claims 4, 8, 12-18, 21 and 22 drawn to an invention nonelected with traverse November 11, 2005. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew D. Kosar whose telephone number is (571)272-0913. The examiner can normally be reached on Monday - Friday 08:00 - 16:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.


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